

(10)



Europäisches Patentamt
European Patent Office
Office européen des brevets

(11) Veröffentlichungsnummer:

0 103 83
A2

(12)

EUROPÄISCHE PATENTANMELDUNG

(21) Anmeldenummer: 83108861.8

(22) Anmeldetag: 12.08.83

(31) Int. Cl.²: C 07 C 91/16
C 07 C 91/30, C 07 C 93/00
C 07 C 93/14, C 07 C 103/2
C 07 C 149/36, C 07 C 149/4
A 61 K 31/135, A 61 K 31/1
A 61 K 31/215, A 23 K 1/16

(30) Priorität: 22.08.82 DE 3234895
22.02.83 DE 3306159

(43) Veröffentlichungstag der Anmeldung:
28.03.84 Patentblatt 84/13

(54) Benannte Vertragsstaaten:
AT BE CH DE FR GB IT LI LU NL SE

(71) Anmelder: BAYER AG
Konzernverwaltung RP Patentabteilung
D-6000 Leverkusen 1 Bayerwerk(DE)

(72) Erfinder: Böehagen, Horst, Dr.
Wiesenstrasse 4
D-6857 Heen(DE)

(72) Erfinder: Stotefuss, Jürgen, Dipl.-Ing.
Parkstrasse 29
D-6857 Heen(DE)

(72) Erfinder: Berachauer, Friedrich, Dr.
Claudiusweg 9
D-6800 Wuppertal(DE)

(72) Erfinder: De Jong, Anna, Dr.
Stockmannsmühle 48
D-6800 Wuppertal 1(DE)

(72) Erfinder: Scheer, Martina, Dr.
Herbert-Katernberg 7
D-6800 Wuppertal 1(DE)

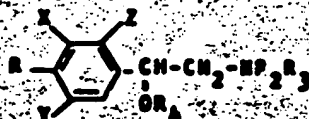
(72) Erfinder: Horstmann, Harald, Dr.
Claudiusweg 19
D-6800 Wuppertal 1(DE)

(72) Erfinder: Seidla, Peter-Rudolf, Dr.
Alte Heide 5d
D-6800 Köln 98(DE)

BEST AVAILABLE COPY

(14) Wachstumsfördernde Phenylethylamin-Derivate.

(17) Die Erfindung betrifft Phenylethylamin-Derivate der allgemeinen Formel I



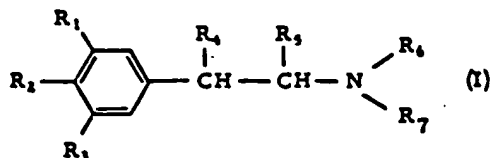
In der die Reste R, R₂, R₃, R₄, X, Y und Z die in der Beschreibung angegebene Bedeutung haben und deren Verwendung als wachstumsfördernde Zusätze in der Tierernährung.

EP 0 103 830 A2

84-076585/13 B05 C03 TROP-22.09.82
TROPONWERKE & GMBH *DE 3234-995-A
22.09.82-DE-234995 (22.03.84) A23k-01/16 A61k-31/13
Sympathomimetic phenethylamine derivs. - used growth promoters
for animals e.g. cattle, birds or fish

C84-032714

The use of cpds. of formula (I) and their
physiologically tolerable salts as growth promoters for
animals is new.



(R₁, R₂ and R₃ are H, OH, alkoxy or hydroxymethyl;
R₄ is H or OH;
R₅ is H, opt. branched or cyclic alkyl or alkenyl, aryl,
acyl or aroyl, the alkyl, alkenyl and aryl residues opt.
being substd. by halogen, OH, alkyl, alkoxy, amino, opt.
substd. phenyl or heteroaryl;
R₆ and R₇ are H, opt. branched or cyclic alkyl, alkenyl.

BC(7-D3, 7-D5, 7-D11, 7-E3, 10-A24, 10-B1A, 10-B1B, 10-B3B, 0;
10-B4B, 10-D3, 12-19)

aryl, acyl, aroyl, mono- or dialkylaminoalkyl, alkoxy-
alkyl, phenoxyalkyl or acyl, the alkyl, alkenyl and aryl
residues opt. being substd. by halogen, amino, alkyl,
alkoxy, OH, acylamino, opt. substd. phenyl or heteroaryl
or NR₆R₇ is an opt. substd. pyrrolidine, piperidine,
piperazine or morpholine residue).

Animal feeds and growth-promoting agents contg. (I)
are also claimed.

USE

For promoting and accelerating growth and improving
feed utilisation in healthy and diseased animals, including
warm blooded animals such as cattle, pigs or sheep, fur
animals and birds (e.g. poultry, cage birds), as well as
cold-blooded animals such as fish or reptiles.

DETAILS

(I) are known cpds. with sympathomimetic activity.
Pref. R₁, R₂ and R₃ are H or OH, R₄ is OH, R₅ is H or
CH₃, and R₆ and R₇ are H or 1-4C alkyl/opt. substd. by
phenyl, phenoxy, hydroxyphenyl or methylenedioxyphenyl
(I) are generally added to feed or drinking water in a

DE3234995

concn. of 0.01-50 (esp. 0.1-10) ppm.

EXAMPLE

A 15-day feeding trial is carried out in rats with
various cpds. (I) including 1-(3,4-dihydroxyphenyl)-2-(1-
methyl-2-(3,4-methylenedioxyphenyl)ethylamino)ethanol
hydrochloride.

In rats fed a diet contg. 25 ppm test cpd., growth is
112%, feed intake 104%, and feed utilisation 92.9% of that
of control animals. (24pp280DAHDwgNo0/0).

BEST AVAILABLE COPY

DE3234995

84-076738/13 B04 D16 OWEL 16.09.82
OWENS-ILLINOIS INC *DE 3329-659-A
16.09.82-US-418884 (22.03.84) A23j-01/18 C07g-07 C12n-09
C12n-11 C12p-21

Imparting enzyme activity to protein - by contacting denatured
protein with immobilised enzyme inhibitor and crosslinking

C84-032764

Prod'n. of a modified protein (I) having
enzymatic activity imitating that of a selected enzyme (II)
is effected by:

- immobilising an inhibitor of (II) on a solid carrier;
- partially denaturing a native protein (III); and
- crosslinking (III) in the presence of the immobilised
inhibitor.

USE/ADVANTAGE

The process can be used to produce enzymatically
active substances from inexpensive proteins, e.g. in
cases where the corresp. natural enzyme is in short
supply or expensive to isolate. The prods. may be used
e.g. as biological catalysts.

DETAILS

(III) may be e.g. bovine serum albumin (BSA) or an
enzyme whose activity is to be modified, e.g. glucoamylase.
The inhibitor is pref. immobilised on a carbohydrate

B(4-B2C, 4-B4A) D(5-A2) 2

carrier (esp. agarose gel) by covalent bonding.

(III) may be denatured thermally or with an aq. soln. of
a chemical denaturant, esp. an inorganic acid, water-
miscible organic solvent or inorganic salt.

The process may be carried out by passing a soln. of
the partially denatured (III) through a column of the
immobilised inhibitor, followed by a soln. of a crosslinking
agent.

EXAMPLE

A 1% BSA soln. was injected into a column of L-tryptophan/agarose gel satd. with 0.01M acetate buffer (denaturant, pH 4.4). A mixt. of 20 ml glutaraldehyde soln. (8%) in 25ml acetate buffer (pH 4.4) was circulated through the column for 90 min.

The prod. was eluted with glycine-HCl buffer (pH 3.0) and pptd. with Tris buffer (pH 7.5). The prod. had esterase activity when tested on α-benzoyl-L-arginine ethyl ester. (91pp367DAHDwgNo0/0).

DE3329659